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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,148	10/01/2003	Stanley Willetts Chapman	21155 US1	8177

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER
WOODWARD, CHERIE MICHELLE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/677,148	**Applicant(s)** CHAPMAN ET AL.	
	Examiner Cherie M. Woodward	**Art Unit** 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2006*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.
  4a) Of the above claim(s) *25-29 and 37-41* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-24 and 30-36* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
  Paper No(s)/Mail Date *12/29/03, 5/14/04*.
4) ☐ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-24 and 30-36) in the reply filed on 5 April 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL.

Formal Matters

2. Claims 1-41 are pending. Claims 25-29 and 37-41 are withdrawn as drawn to non-elected inventions. Claims 1-24 and 30-36 are under examination.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on 29 December 2003 and 14 May 2004 have been considered. The B3 reference (WO 97/20791) in the 29 December 2003 IDS has been lined through and not considered in its entirety. Only the abstract of the WO 97/20791 reference has been considered, as it was the only portion of the reference in English. The entire document will be considered upon the submission of a certified translation in English. Signed copies of the IDS form are attached hereto.

Specification

4. The use of the trademarks ZENAPAX (pp. 21-23, 25-26, and 28) and FUNGIZONE (p. 28) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claims 15, 17, and 30 are objected to because of the following informalities: The claims are missing articles. Claim 15 is missing the word "a" in line 3, prior to the phrase "pharmaceutical composition." Claim 17 is missing the word "the" in line 1, prior to the phrase "second component."

Claim 30 is missing the word "a" in line 10, prior to the phrase "pharmaceutical composition." Appropriate correction is required.

6. Claims 2 and 5 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. Claims 2 and 5 do not further limit the parent claim. The terms fungal and mycotic are synonyms and do not differ in scope (see, e.g. Tortora et al., Microbiology an Introduction, Benjamin Cummings Publishers, 2001, p. 339, second column last paragraph).

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-24 and 30-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for human patients, does not reasonably provide enablement for patients of any other species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims recite a method for treating a patient having a fungal infection, comprising administering to said patient a therapeutically effective amount of an antifungal agent in association with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the infection is a mycotic infection; wherein the monoclonal antibody is a humanized anti-Tac antibody; wherein the monoclonal antibody is daclizumab; wherein the antifungal agent is an antimycotic agent; wherein the antimycotic agent is a polyene antimycotic; wherein the polyene antimycotic is amphotericin B; wherein the antifungal agent is amphotericin B and the monoclonal antibody is daclizumab; wherein the administration of the therapeutically effective amount of amphotericin B and the therapeutically effective amount of daclizumab occurs concomitantly; wherein a part of the therapeutically effective amount of daclizumab is first administered followed by a combination of the remainder of the therapeutically effective amount of daclizumab in association with the therapeutically effective amount of amphotericin B; wherein the amphotericin B is administered intravenously; wherein the amount of amphotericin B is 0.3 to 25 mg/kg per day; wherein daclizumab is administered intravenously; wherein the amount of daclizumab is about 1 mg/kg one to four times per week; a method for treating a patient having a fungal infection comprising administering over a given period of time to the patient (a) a first component consisting of a pharmaceutical composition consisting of an injectable solution containing as an active ingredient an antimycotic agent in a therapeutically effective amount to decrease the severity of the fungal infection and (b) a second component consisting of an injectable solution containing as an active ingredient a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor and inhibits binding of IL-2 to an IL-2 receptor in a therapeutically effective amount to prevent reactions commonly experienced by patients who receive an antimycotic agent, said components being concomitantly administered over a period of time at least sufficient to resolve an invasive fungal infection; wherein the antimycotic agent is amphotericin B; wherein the second component consists of an injectable solution containing as an active ingredient a humanized anti-Tac monoclonal antibody; wherein the anti-Tac monoclonal antibody is daclizumab; a method for treating a patient having a fungal infection comprising concomitantly administering to the patient (i) a first component consisting of an injectable solution containing as an active ingredient amphotericin B, and (ii) a second component consisting of an injectable solution containing as an active ingredient a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the active ingredient of the second component is a humanized anti-Tac antibody; wherein the active ingredient of the pharmaceutical composition of the first component is administered in an approximate amount of 0.3 to 25 mg/kg per day; wherein the active ingredient of the second component is administered in an approximate amount of 1 mg/kg to 2 mg/kg per week; wherein the components are concomitantly administered over a period of time from about 4 weeks to about 8 weeks; wherein the components are concomitantly administered over a period of time of about 8 weeks; a method for treating a patient having a fungal infection comprising administering to the patient over a period of time at least sufficient to resolve an invasive fungal infection, in fourteen day cycles, (a) a first component, delivered on day 1 of each fourteen day cycle, consisting of an injectable solution containing as an active ingredient a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor and inhibits binding of IL-2 to an IL-2R in a therapeutically effective amount to prevent reactions commonly experienced by patients who receive an antifungal agent and (b) a second component, delivered each day of each fourteen day cycle, consisting of a pharmaceutical composition consisting of an injectable solution containing as an active ingredient an antifungal agent in a therapeutically effective amount to decrease the severity of the fungal infection; wherein the antifungal agent is amphotericin B; wherein said monoclonal antibody is an anti-Tac antibody; wherein said anti-Tac antibody is daclizumab; wherein the monoclonal antibody is administered in an amount of about 1 mg/kg to about 2 mg/kg weekly; wherein the antimycotic agent is administered in an amount of about 0.3-25 mg/kg daily; wherein components (a) and (b) are administered for a period of about 4 to 8 weeks.

The nature of the invention is drawn to a method for treating a fungal infection by administering two known compounds, an antifungal and an anti-IL-2p55 monoclonal antibody. The level of skill of those in the art is extremely high due to the complex nature of treating fungal infections and the well-documented toxicity antifungal compounds such as amphotericin B (see i.e. Hoesley et al., Clin Updates Fung Inf, 1999 Jun 2(2) p.1-6, especially p. 1, first paragraph; page 2, second to fourth paragraphs). The nature of the invention is complex, in part, because mammalian cells and fungal cells are both eukaryotic and use the same mechanisms to synthesize proteins and nucleic acids (see, for example, Tortora et al., Microbiology an Introduction, Benjamin Cummings Publisher, 2001, p. 563, second column, first paragraph). Additionally, amphotericin B is capable of irreversibly binding to ergosterol in fungal cytoplasmic membranes, thus increasing membrane permeability and cell death through the leakage of cell contents (see i.e. Hoesley et al., supra, page 2, first full paragraph). However, this mechanism of action makes the drug very toxic to humans and other mammals because amphotericin B also binds mammalian cholesterol (see i.e. Cybulska et al., Acta Biochimica Polonica 2002 49(1):67-75, especially p. 69, first column, second paragraph; p. 72, entire page to p. 74).

There is one working model of a method for treating fungal infections and it is directed only to human subjects (see Example 1, specification, pp. 21-28) No in vitro or in vivo data are show to support the presumption that this method can be used in species other than humans. The antifungal agent amphotericin B is well known to be highly toxic in other mammalian species (see, i.e., Hoesley et al., *supra*, p. 4, first paragraph; and Tortora et al., supra, p. 564, column 1, first paragraph). Additionally, daclizumab is a humanized antibody against a human epitope, the human IL-2p55 receptor subunit.

Humanized monoclonal antibodies are highly species specific (see e.g. Klingbeil et al., Toxicol Pathol 1999 Jan-Feb 27(1):1-3, Abstract only). It is also known that different animal species have different amino acid sequences for the same proteins in humans. As such, concerns have been raised about the effects of monoclonal antibodies used in nonhuman species, particularly as to their pharmacodynamic, pharmacokinetic, and toxicologic profiles (see i.e. Maceria et al., Appl Imunohistochem Mol Morphol 2004 Dec 12(4):360-3, Abstract only). The uncertainty of how nonhuman species will react to humanized monoclonal antibodies, such as daclizumab requires more than mere routine experimentation in order to use daclizumab in nonhuman species. Moreover, it has been shown that combinations of therapies that include decalizumab show variable responsiveness due to differences in toxicity in different species (see i.e. Hyder et al., Toxicology in Vitro 2005 Jun 19(4):541-546, especially p. 541, abstract).

Due to the large quantity of experimentation necessary to determine whether the claimed method is suitable for treatment of non-human species, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention given that animal cells and fungal cells are both eukaryotic and use the same mechanisms to synthesize proteins and nucleic acids, which makes fungal infections especially difficult to treat, the state of the prior art establishing that administration of amphotericin B presents serious toxicity concerns, and the breadth of the claims which fail to recite any particular species of patient to be treated, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "in association with" is unclear. It does not reasonably apprise the skilled artisan of the metes and bounds in which the antifungal agent is to be administered with the IL-2Rp55 antibody.

11. Claims 15-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrases "a given period of time" and "a period of time" are indefinite for failing to specify the metes and bounds of the time period for administration, which appears to be a critical component of the claims.

12. Claims 30-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "delivered each day" (claim 30, lines 4 and 7) is read as "administered each day." The language of the claim, as currently written, is unclear, as there is no reference to "delivery" elsewhere in the claim.

13. Claims 30-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "prevent reactions" is unclear. There is no explanation of what kinds of reactions are to be prevented.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Lai, US Patent 6,649,591 B2 (18 November 2003, publication date 18 April 2002, priority to 10 September 1996).

The claims recite a method for treating a patient having a fungal infection, comprising administering to said patient a therapeutically effective amount of an antifungal agent in association with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the infection is a mycotic infection; wherein the monoclonal antibody is a humanized anti-Tac antibody; wherein the monoclonal antibody is daclizumab; wherein the antifungal agent is an antimycotic agent; wherein the antimycotic agent is a polyene antimycotic; wherein the polyene antimycotic is amphotericin B; wherein the antifungal agent is amphotericin B and the monoclonal antibody is daclizumab.

Lai teaches methods of treatment of subjects suffering from fungal infections (column 11, lines 10-13 and 31-32) with combinatorial therapeutic methods employing an effecting amount of a combination of at least one treating agent useful for the treatment of infections and/or inflammatory conditions and at least one dithiocarbamatie-containing nitric oxide scavenger (column 6, lines 35-44) wherein the expression of inducible nitric oxide synthase and overproduction of nitric oxide (column 14, lines 4-6) is associated with fungal infections (e.g. candidiosis and histoplasmosis) (column 14, lines 22-24). Lai teaches that treatment bay be carried out with anti-cytokine antibodies (column 14, lines 48-50 and column 15, lines 13-19), antifungal therapeutics (column 14, line 62), including amphotericin B (column 17, lines 3-7), and anti-IL-2 monoclonal antibodies/IL-2 receptor antagonists, including daclizumab (column 17, lines 64-65; column 19, lines 62-63), anti-Tac(Fv)-PE40 monoclonal antibodies (column 19, lines 57-58), anti-CD25 monoclonal antibodies and anti-Tac antibodies (column 21, line 54). Lai teaches pharmaceutical formulations in the form of sterile injectable suspension (column 12, lines 66-67) and administration by intravenous delivery (column 26, lines 14-15). Lai teaches all of the limitations of claims 1-8.

16. Claims 1-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Blumberg et al., (US Pregrant Application US2003/0235536 A1, published 25 December 2003, priority to 15 march 2002).

The claims recite a method for treating a patient having a fungal infection, comprising administering to said patient a therapeutically effective amount of an antifungal agent in association with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the infection is a mycotic infection; wherein the monoclonal antibody is a humanized anti-Tac antibody; wherein the monoclonal antibody is daclizumab; wherein the antifungal agent is an antimycotic agent; wherein the antimycotic agent is a polyene antimycotic; wherein the polyene antimycotic is amphotericin B; wherein the antifungal agent is amphotericin B and the monoclonal antibody is daclizumab.

Blumberg et al., teach pulmonary administration of antifungal agents (p. 13, paragraph 0133 and p. 14, paragraph 0137), including amphotericin B (p. 16, paragraph 0165), conjugated (p. 2, paragraph 0011) with FcRn binding partners, including daclizumab (p. 18, Table 1 and p. 21, paragraphs 0223-0225), to treat pathogenic infections wherein the administration is systemic, but directed through the central airways of the lung (paragraph 0070).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hausen et al., (Transplantation 2000 Feb 27 69(4):488-496).

The claims recite a method for treating a patient having a fungal infection, comprising administering to said patient a therapeutically effective amount of an antifungal agent in association with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the infection is a mycotic infection; wherein the monoclonal antibody is a humanized anti-Tac antibody; wherein the antifungal agent is an antimycotic agent.

Hausen et al., teach the treatment of lung allograft patients with a combination of high doses of cyclosporine A, rapamycin, and the chimeric anti-IL-2R CD25 monoclonal antibody, basiliximab (page 1, abstract). Daclizumab is taught on p. 2, fourth full paragraph. Cyclosporin A is a well known antifungal with antifungal and antimycotic properties. For exemplary teaching purposes only, see, for example, Bell et al., (Cornea 1999 May; 18(3):306-13, Abstract only) demonstrated the effectiveness of cyclosporine A against *Aspergillus fumigatus*, *Fusarium oxysporum*, and *Fusarium solani* and Sazykin et al., demonstrated the effectiveness of cyclosporine A against *Aspergillus niger* (Antibiot Khimioter 1994 Jul 39(7):3-9, Abstract only).

Although Hausen et al., do not specifically teach the same patient population as the instant application, due to the high risk for fungal infections following allograft transplant, the populations of Hausen et al., and the instant application overlap (see, for exemplary purposes only, Singh et al., Transplantation 27 March 2004 77:795-800, showing that immunosuppressive agents such as cyclosporine A, tacrolimus, and rapamycin have potent antifungal activity against a number of opportunistic fungi infections in organ transplant recipients). See also, for exemplary purposes only Van Burik, (Curr Opin Infect Dis 2005 18:479-483, showing several high-risk transplant populations that require antifungal prophylaxis due to the predictable development of fungal infection, p. 479, second column, Introduction, and throughout; lung and kidney transplants are taught at p. 479, column 2, first paragraph, p. 482, column 1, last paragraph to column 2, second paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer an antifungal agent with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor and inhibits the binding of IL-2 to an IL-2 receptor. The person of ordinary skill in the art would have been motivated to do so because the antifungal properties of cyclosporine A have been known in the art since 1976 (see e.g. Singh et al., supra, p. 795, column 1, first full paragraph) and would have reasonably expected success because Hausen et al., successfully taught a method of administering a combination of cyclosporine, basiliximab (as well as daclizumab) in lung transplant patients, who are known in the art to be at very high risk for predictable fungal infections following organ transplantation (see Van Burick, *supra*, and Singh et al., *supra*).

21. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trimarchi et al., (Nephron 2001 Apr 87:361-364).

The claims recite a method for treating a patient having a fungal infection, comprising administering to said patient a therapeutically effective amount of an antifungal agent in association with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the infection is a mycotic infection; wherein the monoclonal antibody is a humanized anti-Tac antibody; wherein the monoclonal antibody is daclizumab; wherein the antifungal agent is an antimycotic agent.

Trimarchi et al., teach the treatment of kidney transplant patient with a combination of high doses of cyclosporine A, rapamycin, and the chimeric anti-IL-2R CD25 monoclonal antibody, daclizumab (page 1, abstract). Cyclosporin A is a well known antifungal with inherent antifungal and antimycotic properties. For exemplary teaching purposes only, see, for example, Bell et al., and Sazykin et al., *supra.* See also, for exemplary purposes only Van Burik, (Curr Opin Infect Dis 2005 18:479-483, showing several high-risk transplant populations that require antifungal prophylaxis due to the predictable development of fungal infection, p. 479, second column, Introduction, and throughout; lung and kidney transplants are taught at p. 479, column 2, first paragraph, p. 482, column 1, last paragraph to column 2, second paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer an antifungal agent with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor and inhibits the binding of IL-2 to an IL-2 receptor. The person of ordinary skill in the art would have been motivated to do so because the antifungal properties of cyclosporine A have been known in the art since 1976 (see e.g. Singh et al., supra, p. 795, column 1, first full paragraph) and would have reasonably expected success because Trimarchi et al., successfully taught a method of administering a combination of cyclosporine and daclizumab in kidney transplant patients, who are known in the art to be at very high risk for predictable fungal infections following organ transplantation (see Van Burick, *supra;* Singh et al., *supra;* and Takashai, Nippon Ishinkin Gakkai Sasshi 2001 42(4):201-4, Abstract only).

22. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bumgardner et al., (Transplantation 2001 September 15 72(5):839-845) in view of

The claims recite a method for treating a patient having a fungal infection, comprising administering to said patient a therapeutically effective amount of an antifungal agent in association with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor that inhibits binding of IL-2 to an IL-2 receptor; wherein the infection is a mycotic infection; wherein the monoclonal antibody is a humanized anti-Tac antibody; wherein the monoclonal antibody is daclizumab; wherein the antifungal agent is an antimycotic agent.

Bumgardner et al., teach the treatment of kidney transplant patients with a combination doses of cyclosporine A, azathioprine, corticosteriods, and the chimeric anti-IL-2R CD25 monoclonal antibody, daclizumab (page 1, abstract). Cyclosporin A is a well known antifungal with inherent antifungal and antimycotic properties. For exemplary teaching purposes only, see, for example, Bell et al., and Sazykin et al., supra. See also, for exemplary purposes only Van Burik, (Curr Opin Infect Dis 2005 18:479-483, showing several high-risk transplant populations that require antifungal prophylaxis due to the predictable development of fungal infection, p. 479, second column, Introduction, and throughout; lung and kidney transplants are taught at p. 479, column 2, first paragraph, p. 482, column 1, last paragraph to column 2, second paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer an antifungal agent with a therapeutically effective amount of a chimeric or humanized monoclonal antibody that binds to the p55 subunit of the human IL-2 receptor and inhibits the binding of IL-2 to an IL-2 receptor. The person of ordinary skill in the art would have been motivated to do so because the antifungal properties of cyclosporine A have been known in the art since 1976 (see e.g. Singh et al., supra, p. 795, column 1, first full paragraph) and would have reasonably expected success because Bumgardner et al., successfully taught a method of administering a combination of cyclosporine, daclizumab in kindey transplant patients, who are known in the art to be at very high risk for predictable fungal infections following organ transplantation (see Van Burick, *supra;* Singh et al., *supra*, and Takahashi, *supra*).

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CMW

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600